REMARKS

Reconsideration of the Application is respectfully requested. Upon entry of the foregoing amendment, Claims 1, 4-11, 14-18, 24-30 and 41-46 are presently pending. Claims 31-40 are withdrawn. Claims 1, 11, 14-18 and 24 have been amended. Claims 41-46 have been added. Basis for the amendments and new claims may be found throughout the specification and claims as originally filed. Claims 2-3, 12-13 and 19-23 have been cancelled herein without prejudice or disclaimer. Applicant reserves the right to pursue the subject matter of the cancelled claims in one or more continuation or divisional application. No new matter has been introduced and entry of the amendment is requested.

Objection to the sequence disclosures

The application has been objected to as failing to comply with the requirements of 37 CFR 1.821(a)(1) and (a) (2). The specification has been amended to include SEQ ID NO identifiers consistent with 37 CFR 1.821(a)(1) and (a) (2).

Rejections under 35 U.S.C. § 102

Claims 1-2, 4-5, 8-15 and 20-30 stand rejected under 35 U.S.C. 102(e) as allegedly anticipated by Henderson et al., U.S. Patent Publication No. 2004/0241857. Applicants respectfully submit that the presently claimed invention is not anticipated by Henderson et al.

Henderson et al. is cited as disclosing adenoviral vectors that contain at least one interfering genetic elements (an ITR), at least one transcription unit (an E1b coding sequence) wherein at least one insulating sequence (a termination sequence or polyA sequence for the E1a gene) is located 5' to the transcription initiation site for the E1b gene and 3' to the left hand ITR. Henderson et al. does not describe or suggest an adenoviral vector comprising a left ITR, an E1a

transcription unit and at least one insulating sequence (i.e. a polyA sequence) which is inserted 5' to the transcription initiation site of the E1a transcription unit, as presently claimed. It follows that Henderson et al. does not anticipate nor render obvious the current claims and the rejection should be withdrawn.

Claims 1-2, 4-6, 8-15, 20-22 and 27-30 stand rejected under 35 U.S.C. 102(e) as allegedly anticipated by Tikoo et al., U.S. Patent No. 6,458,586. Applicants respectfully submit that the presently claimed invention is not anticipated by Tikoo et al.

Tikoo et al. is cited as disclosing bovine adenoviral vectors comprising 5' and 3' ITRs, a packaging signal, a gene essential for replication, an SV-40 late polyA sequence linked to a BHV-1 glycoprotein D coding sequence and corresponding viral particles and cells comprising them. Tikoo et al. do not describe a replication conditional adenoviral vector comprising a left ITR, an E1a transcription unit and at least one insulating sequence (i.e. a polyA sequence), which is inserted 5' to the transcription initiation site of the E1a transcription unit and 3' to the left ITR and the adenoviral packaging signal, as presently claimed. It follows that Tikoo et al. does not anticipate nor render obvious the current claims and the rejection should be withdrawn.

Claims 1-5, 8-15, 20-22 and 27-30 stand rejected under 35 U.S.C. 102(e) as allegedly anticipated by Perricaudet et al., U.S. Patent No. 6,420,170. Applicants respectfully submit that the presently claimed invention is not anticipated by Perricaudet et al.

Perricaudet et al. is cited as disclosing adenoviral vectors comprising 5' and 3' ITRs, a packaging signal, a gene essential for replication (E2, E4, etc.), at least one interfering genetic element (an ITR), a transcription unit (such as a heterologous gene of viral origin under control of an inducible promoter) and at least one insulating sequence (or negative regulatory element). Perricaudet et al. discloses replication defective adenoviral vectors that have a deletion in all or part of the E1 gene (see, e.g., column 6, lines 46-65 and figure 1), wherein replication is based on

a "novel" inducible promoter system (see, column 3, lines 63-65). The replication defective adenoviral vectors such as those described by Perricaudet et al. do not describe or suggest replication conditional adenoviral vectors comprising an E1a transcription unit and at least one insulating sequence (i.e. a polyA sequence), which is inserted 5' to the transcription initiation site of the E1a transcription unit and 3' to the left ITR and the adenoviral packaging signal, as presently claimed. As one of skill in the art would appreciate, replication conditional adenoviral vectors rely on selective expression of adenoviral genes in target cells such that they selectively replicate therein. In contrast, replication defective vectors such as those of Perricaudet et al. are defective in one or more adenoviral genes essential for replication such that they can only be propagated in a cell line that complements for the defective gene. It follows that Perricaudet et al. does not anticipate nor render obvious the current claims and the rejection should be withdrawn.

Claims 1-5, 11, 16-18, 20 and 21 stand rejected under 35 U.S.C. 102(e) as allegedly anticipated by Ayares et al., U.S. Patent Publication No. 2004/0241857. Applicants respectfully submit that the presently claimed invention is not anticipated by Ayares et al.

Ayares et al. is cited as disclosing adenoviral vectors with 5' and 3' ITRs, a deleted E1 region and a deleted packaging signal. Ayares et al. do not describe a replication conditional adenoviral vector comprising a left ITR, an E1a transcription unit and at least one insulating sequence (i.e. a polyA sequence), wherein the insulating sequence is inserted 5' to the transcription initiation site of the E1a transcription unit and 3' to the left ITR the adenoviral packaging signal, as presently claimed. It follows that Ayares et al. does not anticipate nor render obvious the current claims and the rejection should be withdrawn.

Claims 1-5, 8-15, 20-22 and 27-30 stand rejected under 35 U.S.C. 102(e) as allegedly anticipated by Lieber et al., U.S. Patent No. 6,686,196. Applicants respectfully submit that the

presently claimed invention is not anticipated by Lieber et al.

Lieber et al. is cited as disclosing adenoviral vectors with left and right ITRs, one or more adenoviral genes essential for replication and a packaging signal that is relocated at the right end of the adenoviral genome, 3' to the termination signal sequence. Lieber et al. do not describe an adenoviral vector comprising an E1a transcription unit and at least one insulating sequence (i.e. a polyA sequence), wherein the insulating sequence inserted 5' to the transcription initiation site of the E1a transcription unit and 3' to the left ITR and the adenoviral packaging signal, as presently claimed. It follows that Lieber et al. does not anticipate nor render obvious the current claims and the rejection should be withdrawn.

Claims 1-2, 4-5, 7-15, 20-22 and 27-30 stand rejected under 35 U.S.C. 102(b) as anticipated by Crystal et al., U.S. Patent No. 6,013,638. Applicants respectfully submit that the presently claimed invention is not anticipated by Crystal et al.

Crystal et al. is cited as disclosing adenoviral vectors comprising a 5' and 3'ITR, a therapeutic gene, a deleted E3 region, at least one transcription unit (a CFTR, pIX, E2 or E4 gene) wherein at least one insulting sequence is located 5' to the transcription initiation site of the transcription unit and 3' to the left hand ITR. Crystal et al. is directed to replication deficient adenoviral vectors for gene transfer into the lungs. Crystal et al. do not describe an adenoviral vector comprising an E1a transcription unit and at least one insulating sequence (i.e. a polyA sequence), wherein the insulating sequence inserted 5' to the transcription initiation site of the E1a transcription unit and 3' to the left ITR and the adenoviral packaging signal, as presently claimed. For the reason set forth above with respect to the rejection over Perricaudet et al. one of skill in the art would appreciate that the replication deficient adenoviral vectors of Crystal et al. are not the same as, nor do they suggest the replication competent vectors of the present invention. It follows that Crystal et al. does not anticipate nor render obvious the current claims

and the rejection should be withdrawn.

Claims 11-5, 8-15, 20-21 and 28-30 stand rejected under 35 U.S.C. 102(b) as anticipated by Vassaux et al. (Gene Therapy, 1999). Applicants respectfully submit that the presently claimed invention is not anticipated by Vassaux et al.

Vassaux et al. is cited as disclosing adenoviral vectors comprising left and right ITRs, a packaging signal, an insulating sequence (bovine growth hormone transcription stop signal), an E1a expression cassette containing a TK polyA signal and genes essential for replication.

Vassaux et al. discloses replication-defective, recombinant, E1-deleted type 5 adenovirus. Vassaux et al. do not describe an adenoviral vector comprising an E1a transcription unit and at least one insulating sequence (i.e. a polyA sequence), wherein the insulating sequence inserted 5' to the transcription initiation site of the E1a transcription unit and 3' to the left ITR and the adenoviral packaging signal, as presently claimed. For the reason set forth above with respect to the rejection over Perricaudet et al. one of skill in the art would appreciate that the description for the replication deficient adenoviral vectors of Vassaux et al. does not anticipate nor render obvious the current claims. Accordingly, the rejection should be withdrawn.

Double patenting

Claims 1, 3-5, 8-13, 15-25 and 27-30 have been provisionally rejected under the judicially created doctrine of obviousness type double patenting as being unpatentable over Claims 1-11, 13-14, 16-45, 58-59, 62-64 and 67-83 of copending Application No. 10/081,969 ("the '969 application").

Applicants respectfully submit that the presently claimed invention is not made obvious by the claims of the cited patents. However, in order to further prosecution, Applicants proffer the filing of a terminal disclaimer will be considered upon indication of otherwise allowable

subject matter.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 15 and 19 (and dependent claims) are rejected as vague for a lack of antecedent basis for the term "the termination signal sequence" in Claim 11. Claim 15 has been amended to depend from Claim 25 and now recites that "said insulating sequence is a termination signal sequence" thereby providing proper antecedent basis to obviate the rejection. It is respectfully submitted that this rejection has been rendered moot with respect to Claim 19 by cancellation of Claim 19 herein.

Claims 17 and 18 are rejected as vague in that it is allegedly unclear as to what nucleotides are being deleted. Claims 17 and 18 have been amended and no longer recite the term "the termination signal sequence" rendering the rejection moot.

CONCLUSION

In light of the above, Applicants submit that this application is now in condition for allowance and therefore request favorable consideration. If any issues remain which the Examiner feels may be best resolved through a personal or telephonic interview, the Examiner is respectfully requested to contact Applicants' counsel, Linda R. Judge at (415) 836-2586.

Respectfully submitted,

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